



NOTES SPIROCHETES

MICROBE OVERVIEW

Morphology

- Thin-walled, Gram-negative flexible spiral rods
- Length: 5–250µm; diameter: 0.1–0.6µm
- Unique double membrane separated by periplasmic space

- Corkscrew-like motility via axial filament situated lengthwise between inner and outer membranes (endoflagella)

Replication

- **Reproduction:** sexual transverse binary fission

BORRELIA BURGDORFERI (LYME DISEASE)

osms.it/lyme-disease

PATHOLOGY & CAUSES

- An obligate parasite that **causes Lyme disease**, a systemic inflammatory disease
- Non-spore forming
- Life cycle includes mammals, birds, and ticks (genus *Ixodes*), principally in North America
- Killed when exposed to hypotonic or hypertonic environments, drying, disinfectants (e.g. bleach), or temperatures > 50°C/122°F
- Transmission
 - Via tick bite → enters blood → spreads to tissues and organs; especially joints, heart, nervous system
- Infection progresses through **three stages**
 1. **Localized** disease (occurs 3–30 days after exposure)
 2. **Disseminated** disease (days to months after exposure; multisystem involvement)
 3. **Late/chronic** disease (months to years after exposure)

RISK FACTORS

- Exposure to ticks in endemic areas
 - Living in areas bordering forests
 - Outdoor employment, recreation
- Most cases occur in late spring to summer

COMPLICATIONS

- Meningitis, **cranial neuropathy**
- Lyme **carditis**
 - AV block, myopericarditis
- Chronic joint inflammation
- Post-Lyme disease syndrome

SIGNS & SYMPTOMS

Early signs/symptoms of localized disease

- Erythema migrans (EM) rash
 - Non-painful, gradually expanding “bull’s-eye” rash appearing at the site of tick bite; feels warm to palpation; may itch

VISIT...

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- Constitutional
 - Low grade fever, chills, headache, fatigue, myalgia, arthralgia, lymphadenopathy

Disseminated signs/symptoms

- Severe headaches and neck stiffness
- Formation of additional EM
- Joint pain and swelling; especially knees, other large joints
- Facial palsy
- Palpitations (Lyme carditis)
- Episodic dizziness, dyspnea
- Pain
 - Shooting pains, numbness, or tingling in the hands or feet
- Short-term memory loss

Late/chronic disease

- Presence of nonspecific symptoms (e.g. headache, fatigue, joint pain) that persists after treatment for Lyme disease



Figure 97.1 A bulls-eye-shaped rash, known as erythema migrans, at the site of infection with *Borrelia burgdorferi*, the causative agent of Lyme disease.

DIAGNOSIS

LAB RESULTS

CDC testing criteria

- Two tiered testing for lyme disease
 - **First test:** enzyme immunoassay (EIA) or immunofluorescence assay (IFA)
 - **Second test (as needed):** IgM and/or IgG western blot

Other laboratory findings

- Blood chemistry
 - ↑ ESR, serum creatine phosphokinase, aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT)
- Blood studies
 - Anemia, leukocytosis, thrombocytopenia

OTHER DIAGNOSTICS

- History of exposure to ticks in an endemic area and characteristic clinical presentation

TREATMENT

MEDICATIONS

- Antibiotics
 - Doxycycline, amoxicillin, or cefuroxime axetil

BORRELIA SPECIES (RELAPSING FEVER)

osms.it/borrelia-species

PATHOLOGY & CAUSES

- Relapsing fever: bacterial infection caused by *Borrelia spirochetes*

Tick-borne relapsing fever (TBRF)

- Endemic
- Found in endemic areas
 - Mountainous areas of North America, plateau regions of Mexico, Central and South America, Mediterranean, central Asia, Africa
- Caused primarily by *Borrelia hermsii*, *Borrelia turicatae*, *Borrelia parkeri* in North America
- Spread by soft tick species *Ornithodoros parkeri* and *Ornithodoros turicata*
- Risk factors
 - Occupying rodent-infested cabins, caves, or other dwellings
 - Camping near rodent nests
- Tick attaches to human host (usually at night during sleep) → bites and feeds on blood → saliva and spirochete enter host's circulation

Louse-borne relapsing fever (LBRF)

- Epidemic
- Caused by *Borrelia recurrentis*
- Spread person-to-person via body louse
- Risk factors
 - Primarily seen in low resource countries
 - Famines, wars; causes epidemics among refugees, migrant populations
 - Homelessness (exposure to lice)
 - Poor hygiene
- *B. recurrentis* grows in the body cavity *Pediculus humanus corporis* → human host crushes louse/lice feces with fingers → spirochete enters either through bite site, through breaks in the skin caused by scratching, or through conjunctiva when

fingers touch eyes

After entry into human host

- Spirochete divides every 6–12 hours (can number up to 106–108 per mL) → leaves blood and enters tissues: brain, eye, inner ear, liver, heart, testes, and other organs

Pattern of intermittent illness

- Relapsing fever caused by spirochetemia
- Characterized by recurrent episodes of fever and constitutional symptoms with intermittent periods of general well-being
 - Interval range between fevers is 4–14 days
 - Pattern of intermittent illness caused by outer membrane lipoproteins called variable major proteins (VMPs)
 - Employed as multiphasic antigens to evade host adaptive immunity
 - TBRF: multiple febrile periods last 1–3 days each
 - LBRF: first episode lasts 3–6 days, followed by a single milder episode

Complications

- Neurological
 - Meningitis, subarachnoid hemorrhage, cranial nerve neuritis, Bell's palsy, hearing loss
- Ocular
 - Iridocyclitis, panophthalmitis, vision loss
- Cardiac
 - Myocarditis, cardiac failure
- Respiratory
 - Bronchopneumonia, acute respiratory distress syndrome
- Hematologic
 - Thrombocytopenia
- Other
 - Hepatitis, splenic rupture
- During pregnancy

- Spontaneous abortion, prematurity, neonatal death
- Jarisch–Herxheimer reaction
 - During treatment with antibiotics → release of proinflammatory cytokines triggered by products released from dead microbes

SIGNS & SYMPTOMS

- Characteristics of febrile episodes
 - Sudden onset of high fever → crisis phase: chills, ↑↑ temperature, ↑ HR, ↑ BP → diaphoresis, ↓ fever, ↓ BP
 - ↑ mortality during crisis and immediate aftermath
- Constitutional
 - Sudden onset of high fever and chills; followed by headache, myalgia, arthralgia, nausea
- Neurologic
 - Dizziness, delirium, stupor, facial palsy
- Cardiac
 - Prolonged QTc interval.
- Respiratory
 - Nonproductive cough, signs of respiratory distress
- Hematologic
 - Epistaxis, petechiae, ecchymoses, blood-tinged sputum
- Other
 - Hepatomegaly, abdominal pain, photophobia, skin rash

DIAGNOSIS

LAB RESULTS

Visualization of microbe

- Blood: thick or thin smears
 - Giemsa, Wright, or acridine orange stain
 - Direct or indirect immunofluorescence
 - Phase contrast or dark field microscopy
- PCR, culture, serology
- Tissue specimen
 - Silver stain (e.g. Warthin-Starry, modified Dieterle)
 - Immunofluorescence

TREATMENT

MEDICATIONS

- Antibiotics
 - Penicillin G, ceftriaxone, doxycycline

OTHER INTERVENTIONS

Prevention

- Avoidance and eradication of vector

LEPTOSPIRA

osms.it/leptospira

PATHOLOGY & CAUSES

- A spirochete that causes the disease **leptospirosis**
 - AKA **Weil's disease**, Weil–Vasiliev disease, swineherd's disease, rice-field fever, waterborne fever, nanukayami fever, cane-cutter fever, swamp fever, mud fever, Stuttgart disease, canicola fever
- Infected mammal excretes microbe in urine which remains viable in stagnant water and wet soil → environmental exposure by humans → microbe usually enters via non-intact skin, mucous membranes, or conjunctivae (rarely via contaminated food, water, or aerosols)
- Effects of microbe
 - Damages blood vessel endothelium → organ damage
 - Inhibits the $\text{Na}^+\text{-K}^+\text{-Cl}^-$ cotransporter activity in the thick ascending limb of Henle → hypokalemia, hyponatremia

COMPLICATIONS

- Electrolyte imbalance, kidney failure
- Hepatitis, hepatic hemorrhage
- Aseptic meningitis
- Pulmonary hemorrhage, acute respiratory distress syndrome (ARDS)
- Uveitis, optic neuritis
- Myocarditis
- Rhabdomyolysis

SIGNS & SYMPTOMS

- Variable clinical course
 - Ranges from mild disease that resolves uneventfully to severe and potentially fatal
- Common symptoms
 - Abrupt onset of **fever**, **chills**
 - Headache

- Nonproductive cough
- Pharyngitis
- **Myalgias**, arthralgias
- **Conjunctival suffusion** (redness without exudate)
- Lymphadenopathy
- **Jaundice**
- Uremia, bacteremia, oliguria, hypokalemia

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Nodular densities, consolidation; may have a ground-glass appearance

LAB RESULTS

- Identification of microbe
 - PCR, ELISA, microscopic agglutination
- Other laboratory studies
 - Leukocytosis with left shift
 - Hypokalemia, hyponatremia
 - ↑ hepatic transaminases, ↑ direct bilirubin
 - **Urinalysis**: proteinuria, pyuria, granular casts, hematuria, ↑ creatine kinase
 - CSF: neutrophilic pleocytosis, ↑ protein

OTHER DIAGNOSTICS

- History and physical examination

TREATMENT

MEDICATIONS

- Antibiotics
 - Doxycycline (mild cases), penicillin (severe cases)

OTHER INTERVENTIONS

- Address complications
- Prevention
 - Avoidance of potential infectious sources of infection, domestic animal vaccination

TREPONEMA PALLIDUM (SYPHILIS)

osms.it/syphilis

PATHOLOGY & CAUSES

- The spirochete bacterium that causes syphilis, a localized and systemic disease
- Transmission
 - Sexually:** by direct contact with an infectious lesion (primarily) → enters via microscopic abrasions
 - Perinatally:** crosses placenta easily → congenital syphilis
- Progresses through stages
 - Primary:** localized sores (chancre) appear after about three weeks at site of infection
 - Secondary:** 2–8 weeks after chancre resolution, hematogenous bacterial dissemination causes systemic symptoms
 - Latent:** asymptomatic
 - Tertiary (late):** organ damage develops 10–30 years after initial infection
- Neurosyphilis and ocular syphilis can occur at any stage
 - Neurosyphilis begins when the microbe invades the CSF

RISK FACTORS

- Unprotected sex
- Multiple sexual partners
- Biologically male
- Biologically-male individuals engaging in same-sex sexual contact (MSM)
- IV drug use
- Existing sexually-transmitted disease, especially HIV

COMPLICATIONS

- Cardiovascular:** syphilitic aortic aneurysms, dilated aorta, aortic valve regurgitation; coronary artery narrowing
- Congenital syphilis:** hemolytic anemia, deafness, keratitis, periostitis
- Neurosyphilis:** dementia, meningitis, brain or spinal cord ischemia/infarction, seizures, ischemic stroke
- Ocular syphilis:** uveitis, vitritis, retinitis, optic neuropathy, blindness
- Otosyphilis:** hearing loss, tinnitus

SIGNS & SYMPTOMS

Stages

- Presentation will vary according to stage of disease
- Primary
 - Chancre:** painless ulcers at inoculation site (in contrast to painful lesions seen in genital herpes or chancroid)
 - Single or multiple; usually firm, round, painless
 - Heals with or without treatment; treatment prevents progression to secondary stage
- Secondary
 - May be asymptomatic
 - Rash:** diffuse rough, reddish-brown maculopapular on extremities, palms of hands and/or soles of feet, back; raised, gray-whitish lesions on mucous membranes
 - Condylomata lata**

- Myalgia
- Fatigue
- Lymphadenopathy
- Fever
- “Moth-eaten” alopecia
- Resolves without treatment; treatment prevents progression to latent and tertiary stages
- Latent
 - Positive serology; asymptomatic
- Tertiary (late)
 - **Gummas**: non-cancerous, granulomatous growths on internal organs, bones, skin; more common in HIV-infected individuals
 - Evidence of organ involvement; charcot joints, **aortitis** (due to destruction of vasa vasorum)

Complications

- Neurosyphilis
 - **Meningitis**: headache, nausea and vomiting, stiff neck
 - **Tabes dorsalis**: muscle weakness, locomotor **ataxia**, ↓ proprioception, incoordination
 - General paresis (paralytic dementia)
 - Facial and limb hypotonia, intention tremors
 - Forgetfulness, personality changes
- Ocular syphilis
 - ↓ visual acuity; loss of vision
 - **Argyll Robertson pupil**: small pupils that constrict poorly in response to direct light

Congenital syphilis

- Presents with vesicular/bullous rash, rhinitis, hepatosplenomegaly, jaundice, and pseudoparalysis

DIAGNOSIS

LAB RESULTS

- Identification of microbe
- Serum nontreponemal tests (may be nonreactive in late neurosyphilis)
 - Venereal disease research laboratory (VDRL)
 - Rapid plasma reagin (RPR)

- Serum treponemal tests
 - Fluorescent treponemal antibody absorption (FTA-ABS)
 - Treponema pallidum particle agglutination assay (TPPA)
 - Syphilis enzyme immunoassays (EIAs)
- If neurologic symptoms, lumbar puncture and CSF examination
 - ↑ lymphocytes, ↑ protein
 - **CSF-VDRL** reactivity

OTHER DIAGNOSTICS

- History and physical examination



Figure 97.2 A painless penile chancre, seen here, is the clinical manifestation of primary syphilis.



Figure 97.3 Condylomata lata, seen here, are the clinical manifestation of secondary syphilis.

TREATMENT

MEDICATIONS

- Parenteral (IM/IV) penicillin G
 - Doxycycline or tetracycline (PO);
 - ceftriaxone (IM, IV) if penicillin allergy

OTHER INTERVENTIONS

- Treat partners
- Screening during first prenatal visit (VDRL or RPR)

SPIROCHETES OVERVIEW

	VISUALIZATION	RESERVOIR(S)	MODE OF TRANSMISSION
BORRELIA BURGDORFERI (LYME DISEASE)	Visualized with silver stains or immunofluorescence	Small mammals and birds	Arthropod vector: <i>Ixodes ricinus</i> tick bite
BORRELIA HERMSII, BORRELIA TURICATAE, BORRELIA PARKERI (RELAPSING FEVER)	Visualized under light microscopy with Gemisa, Wright, acridine orange, or other stains	Ticks (TBRF): tree squirrels, chipmunks, ground squirrels, prairie dogs, burrowing owls, wild/domestic pigs, bats Human body louse (LBRF) (<i>Pediculus humanus corporis</i>)	Arthropod vector: <i>B. hermsii</i>, <i>B. turicatae</i>, <i>B. parkeri</i> tick bite Person-person via human body louse (arthropod vector) via <i>B. recurrentis</i> Transplacental transmission also possible
LEPTOSPIRA INTERROGANS (LEPTOSPIROSIS)	Does not appear on Gram-stained smear Visualized by immunofluorescence, dark field microscopy, silver stain Distinct morphological feature: question mark-shaped hook at end of the bacterium	Various mammals; e.g. rodents (most common), cattle, swine, dogs, horses, sheep, goats	Incidental environmental exposure to contaminated sources; e.g. animal urine, contaminated water or soil, infected animal tissue
TREPONEMA PALLIDUM (SYPHILIS)	Does not appear on Gram-stained smear Visualized by immunofluorescence or dark field microscopy	Humans	Intimate contact Transplacental